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08/907,041	08/06/1997	JOEL S. GREENBERGER	76333/103	7766

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EXAMINER

CHEN, SHIN LIN

ART UNIT PAPER NUMBER

1632

DATE MAILED: 12/15/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

08/907,041

Applicant(s)

GREENBERGER, JOEL S.

Examiner

Shin-Lin Chen

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 September 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-32 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-32 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

Applicant's amendment filed 9-15-03 has been entered. Claims 1-32 are pending and under consideration.

Specification

Applicant amended the specification on page 1 by inserting a paragraph regarding cross-reference to application No. 08/136,079, however, the filing date of application No. 08/136,079 is October 15, 1993 **not 1995**. Appropriate correction is required. Further, the amendment filed 7-24-02 has already inserted such paragraph regarding application No. 08/136,079. It is confusing why such paragraph is inserted twice on page 1 of the specification.

Priority

1. It is noted that this application appears to claim subject matter disclosed in prior Application No. 09/136,079, filed 10-15-93 and 08/484,836, filed 6-7-95. A reference to the prior application must be inserted as the first sentence of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e) or 120. See 37 CFR 1.78(a). For benefit claims under 35 U.S.C. 120, **the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of all nonprovisional applications**. Also, the current status of all nonprovisional parent applications referenced should be included.

Double Patenting

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. Claims 1-32 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-25 of U.S. Patent No. 5,599,712(A). Although the conflicting claims are not identical, they are not patentably distinct from each other because although drawn to different scope, they encompass the same invention and obvious variants thereof.

The claimed invention of the present application is drawn to a method for protecting a subject against an agent that elicits toxic species including free radicals, superoxide anions, or heavy metal cations, said method comprising the steps of administering to said subject a pharmaceutical composition comprising a polynucleotide that encodes a protein capable of neutralizing or eliminating said toxic species and is transiently expressed in said subject, wherein said administering is a local administration at the site to be protected from irradiation, and said pharmaceutical composition.

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The claims of '712 are drawn to a method for protecting a **cancer** subject against an agent that elicits free radicals, superoxide anions, or heavy metal cations, said method comprising the steps of administering **directly to the site of the tumor** in said subject a pharmaceutical composition comprising a polynucleotide that encodes a **gamma glutamyl transpeptidase, a manganese superoxide dismutase, or a metallothionein**, transiently expressed in said subject, and said pharmaceutical composition.

The claims of the present application clearly encompass the claims of '712. Local administration to the site to be protected from irradiation encompass direct administration to the site of the tumor and it would have been obvious to one of ordinary skill in the art. Claims 17 and 18 of the present application specify the polynucleotide is under the control of an inducible or radioinducible transcriptional regulatory sequence, and claim 30 specifies the polynucleotide is stably integrated into the genome of the subject. Since the polynucleotide is intended to be expressed in the subject, it would have been obvious for one of ordinary skill at the time of the invention to use a regulatory sequence either inducible or not inducible to activate the expression of the polynucleotide in the subject, and the use of inducible or not inducible regulatory sequence depends on the intended targeted tissue(s) or organ(s) of the subject. Further, the integration of the polynucleotide into the genome of the cell of a subject also would have been obvious for one of ordinary skill at the time of the invention because whether the polynucleotide would integrate into the genome of a cell depends on the type of the vector and the component within said vector used. Thus, claims 1-31 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-25 of U.S. Patent No. 5,599,712(A).

4. Claims 1-26 and 30-32 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-23 of U.S. Patent No. 6,221,848 ('848). Although the conflicting claims are not identical, they are not patentably distinct from each other because although drawn to different scope, they encompass the same invention and obvious variants thereof.

The claimed invention of the present application is drawn to a method for protecting a subject against an agent that elicits toxic species including free radicals, superoxide anions, or heavy metal cations, said method comprising the steps of administering to said subject a pharmaceutical composition comprising a polynucleotide that encodes a protein capable of neutralizing or eliminating said toxic species and is transiently expressed in said subject, wherein said administering is a local administration at the site to be protected from irradiation.

Claims 1-23 of '848 is directed to a method for protecting cells of the oral cavity, oropharynx, esophagus, small intestine or colon in a mammalian subject from an agent that elicits production of a toxic species including free radicals, superoxide anions, or heavy metal cations, said method comprising administering in vivo to normal cells of the oral cavity, oropharynx, esophagus, small intestine or colon at a site remote from a site to be treated by said agent, a protective pharmaceutical composition comprising a polynucleotide encoding a protein that neutralizes or eliminates said toxic species.

Local administering at the site to be protected from irradiation to protect a subject encompasses administering in vivo to normal cells of the oral cavity, oropharynx, esophagus, small intestine or colon at a site remote from a site to be treated by agent that elicits toxic species to protect normal cells and it would have been obvious to one of ordinary skill in the art. The

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integration of the polynucleotide into the genome of the cell of a subject also would have been obvious for one of ordinary skill at the time of the invention because whether the polynucleotide would integrate into the genome of a cell depends on the type of the vector and the component within said vector used. Thus, claims 1-32 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-23 of U.S. Patent No. 6,221,848(B1).

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claim 27 remains rejected under 35 U.S.C. 102(b) as being anticipated by Cousens et al., 1988 (US 4,751,180) and is repeated for the reasons set forth in the preceding Official action mailed 5-13-03. Applicant's arguments filed 9-15-03 have been fully considered but they are not persuasive.

Applicant argues that TE buffer is not considered a pharmaceutically acceptable vehicle and yeast expression plasmid in Tris buffer is not a pharmaceutical composition (amendment, p. 5, 6). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 5-13-03. It should be noted that the term “pharmaceutical” in “pharmaceutical composition” does not carry weight in 102(b) or 103(a) rejection of a product or composition claim. The specification of the present application fails to specifically define the phrase

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“pharmaceutically acceptable vehicle”. Water and PBS buffer can be considered pharmaceutically acceptable vehicles and TE buffer or Tris buffer also can be considered a pharmaceutically acceptable vehicle. The use of Tris buffer in laboratory applications, such as in situ hybridization, in vitro diagnostic assays, and as an electrophoresis buffer, does not mean that Tris buffer can not be used as a pharmaceutically acceptable vehicle. It was very well known in the art to use TE buffer as DNA storage buffer. Further, since the term “pharmaceutical” in “pharmaceutical composition” does not carry weight in 102(b) or 103(a) rejection of a product or composition claim, it is irrelevant whether the yeast expression plasmid is used in a pharmaceutical composition or is used for preparing a polypeptide. Thus, claim 27 remains rejected under 35 U.S.C. 102(b).

7. Claims 27 and 28 remain rejected under 35 U.S.C. 102(b) as being anticipated by Hartman et al., 1988 (EP 0284105) and is repeated for the reasons set forth in the preceding Official action mailed 5-13-03. Applicant's arguments filed 9-15-03 have been fully considered but they are not persuasive.

Applicant argues that buffer solution containing the expression plasmid is not mentioned in the Hartman reference and even there is a buffer solution containing said plasmid, Hartman does not teach its use in a “pharmaceutical composition” (amendment, p. 6, 7). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 5-13-03 and the reasons set forth above under 35 U.S.C. 102(b) rejection over Cousens. Since the buffer solution used to store plasmid is very well known in the art, it is common that the buffer solution containing the plasmid was not mentioned in journal publications. Hartman teaches preparation

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of plasmid pMSE-4 and transfection of E. coli cells with said plasmid. Therefore, plasmid pMSE-4 is stored in a DNA buffer solution and said buffer solution is considered a pharmaceutically acceptable vehicle.

8. Claims 27 and 28 remain rejected under 35 U.S.C. 102(b) as being anticipated by Ishiye et al., 1992 (FEMS Microbiology Letters, Vol. 97: 235-241) and is repeated for the reasons set forth in the preceding Official action mailed 5-13-03. Applicant's arguments filed 9-15-03 have been fully considered but they are not persuasive.

Applicant argues that buffer solution containing the expression plasmid is not mentioned in the Ishiye reference and even there is a buffer solution containing said plasmid, Ishiye does not teach its use in a "pharmaceutical composition" (amendment, p. 6, 7). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 5-13-03 and the reasons set forth above under 35 U.S.C. 102(b) rejections. Since the buffer solution used to store plasmid is very well known in the art, it is common that the buffer solution containing the plasmid was not mentioned in journal publications. Ishiye teaches preparation of plasmid pGGT298trp and transfection of E. coli HB101 cells with said plasmid. Therefore, plasmid pGGT298trp is stored in a DNA buffer solution and said buffer solution is considered a pharmaceutically acceptable vehicle.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

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(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. Claims 27 and 29 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Hartman et al., 1988 (EP 0284105) in view of Nabel et al., 1994 (Anals New York Academy of Sciences, Vol. 714, p. 247-252) and is repeated for the reasons set forth in the preceding Official action mailed 5-13-03. Applicant's arguments filed 9-15-03 have been fully considered but they are not persuasive.

Applicant argues that Hartman does not teach using a polynucleotide as a pharmaceutical composition and one skilled in the art would not have been motivated to use expression vector of Hartman for delivery *in vivo* (amendment, p. 7). This is not found persuasive because of the reasons set forth in the preceding Official action mailed 5-13-03 and the reasons set forth above under 35 U.S.C. 102(b) rejections. As discussed above, the term "pharmaceutical" in "pharmaceutical composition" does not carry weight in 102(b) or 103(a) rejection of a product or composition claim. The specification of the present application fails to specifically define the phrase "pharmaceutically acceptable vehicle". The buffer solution containing the plasmid taught by Hartman is considered a pharmaceutically acceptable vehicle. Hartman teaches construction of a plasmid pMSE-4 containing a human manganese superoxide dismutase (hMnSOD) coding region under the control of lambda P_L promoter, and use of said plasmid to transfect *E. coli* cells for producing recombinant hMnSOD. Nabel teaches using retrovirus, adenovirus, adenoviral conjugates, and cationic liposomes for delivery of foreign DNA into vascular cells *in vitro*. One of ordinary skill in the art at the time of the invention would have been motivated to substitute the plasmid as taught by Hartman with adenovirus vector or liposome as taught by Nabel in order

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to introduce the human MnSOD into target cells, such as vascular cell, in vitro with reasonable expectation of success. Thus, claims 27 and 29 remain rejected under 35 U.S.C. 103(a).

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shin-Lin Chen whose telephone number is (703) 305-1678. Due to the move of USPTO to new site in Alexandria, Virginia, examiner's telephone number will be changed to (571) 272-0726 **after January 12, 2004**. The examiner can normally be reached on Monday to Friday from 9:30 am to 6 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds can be reached on (703) 305-4051. The fax phone number for this group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist, whose telephone number is (703) 308-0196.



Shin-Lin Chen, Ph.D.